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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS 11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 12	Apr 08	"Ask CAS" for self-help around the clock
NEWS 13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 14	Apr 09	ZDB will be removed from STN
NEWS 15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 15:36:26 ON 19 APR 2002

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 18 APR 2002 HIGHEST RN 406160-25-6
DICTIONARY FILE UPDATES: 18 APR 2002 HIGHEST RN 406160-25-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

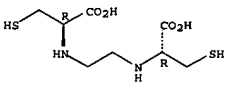
```
=> e ethylenedicysteine
E1            3     ETHYLENEDICYCLOPENTADIENYL/BI
E2            3     ETHYLENEDICYCLOPENTADIENYLENE/BI
E3            1 --> ETHYLENEDICYSTEINE/BI
E4            1     ETHYLENEDIEPHEDRIN/BI
E5            1     ETHYLENEDIEPHEDRINATO/BI
E6            2     ETHYLENEDIGLUC/BI
E7            2     ETHYLENEDIGLUCAMIDE/BI
E8            1     ETHYLENEDIGLUTAM/BI
E9            1     ETHYLENEDIGLUTAMIC/BI
E10           1     ETHYLENEDIGLUTAR/BI
E11           1     ETHYLENEDIGLUTARIMIDE/BI
E12           2     ETHYLENEDIGLYC/BI

=> s e3
L1            1 ETHYLENEDICYSTEINE/BI

=> d
```

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 14344-48-0 REGISTRY
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cysteine, N,N'-ethylenedi- (6CI)
CN Cysteine, N,N'-ethylenedi-, L- (8CI)
OTHER NAMES:
CN **L,L-Ethylenedicysteine**
CN N,N'-1,2-Ethanediylbis-L-cysteine
CN N,N'-Ethylenedi-L-cysteine
FS STEREOSEARCH
DR 378230-72-9
MF C8 H16 N2 O4 S2
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

43 REFERENCES IN FILE CA (1967 TO DATE)
15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
43 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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=>

=> fil .search
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       6.34       6.55

FILE 'MEDLINE' ENTERED AT 15:37:28 ON 19 APR 2002

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FILE 'USPATFULL' ENTERED AT 15:37:28 ON 19 APR 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

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=> s l1
L2          49 L1

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           45 DUP REM L2 (4 DUPLICATES REMOVED)

=> s l2 and (anti(w)cancer? or dna or anti(w)metabolit? or tumor? or tumour? or
folate? or apoptot? or hypoxia? or peptide? or nucleotid? or organ? or antibiotic?
or anti(w)fungal? or antibod? or glutamat? or glucos?)
   3 FILES SEARCHED...
L4          16 L2 AND (ANTI(W) CANCER? OR DNA OR ANTI(W) METABOLIT? OR TUMOR?
               OR TUMOUR? OR FOLATE? OR APOPTOT? OR HYPOXIA? OR PEPTIDE? OR
               NUCLEOTID? OR ORGAN? OR ANTIBIOTIC? OR ANTI(W) FUNGAL? OR ANTIBO
               D? OR GLUTAMAT? OR GLUCOS?)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5           15 DUP REM L4 (1 DUPLICATE REMOVED)

=> d ibib ab hitstr 1-
YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):y
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L5 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:885838 CAPLUS
DOCUMENT NUMBER: 136:17356
TITLE: Ethylenedicysteine (ec)-drug conjugates, compositions and methods for tissue specific disease imaging
INVENTOR(S): Yang, David J.; Liu, Chun-wei; Yu, Dong-fang; Kim, E. Edmund
PATENT ASSIGNEE(S): Board of Regents The University of Texas System, USA
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001091807	A2	20011206	WO 2001-US18060	20010601

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

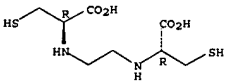
PRIORITY APPLN. INFO.: US 2000-587583 A1 20000602
US 2000-599152 A1 20000621

AB The invention provides, in a general sense, a new labeling strategy employing 99mTc chelated with ethylenedicysteine (EC). EC is conjugated with a variety of ligands and chelated to 99mTc for use as an imaging agent for tissue-specific diseases. The drug conjugates of the invention may also be used as a prognostic tool or as a tool to deliver therapeutics to specific sites within a mammalian body. Kits for use in tissue-specific disease imaging are also provided.

IT **14344-48-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of radiolabeled ethylenedicysteine-drug conjugates for **tumor** targeting)

RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

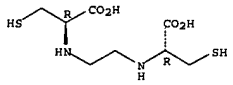
Absolute stereochemistry.



IT **14344-48-0DP**, Annexin V conjugate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

L5 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)
(prepn. of radiolabeled ethylenedicysteine-drug conjugates for **tumor** targeting)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



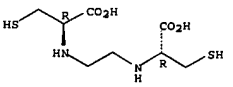
L5 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:293410 CAPLUS
DOCUMENT NUMBER: 135:376612
TITLE: Potential 166Ho radiopharmaceuticals for intravascular radiation therapy (IVRT)-I : [166Ho] holmium labeled ethylene dicysteine
AUTHOR(S): Chakraborty, S.; Unni, P. R.; Banerjee, S.; Samuel, G.; Das, T.; Sarma, H. D.; Ramamoorthy, N.; Pillai, M. R. A.
CORPORATE SOURCE: Radiopharmaceuticals Division, Bhabha Atomic Research Centre, Mumbai, 400085, India
SOURCE: Nuclear Medicine and Biology (2001), 28(3), 309-317
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The use of .beta.- emitting radionuclides in the control of restenosis in post angioplasty patients is currently under intense investigation at many leading cardiovascular research centers. 32P coated metallic stents, 192Ir wire source and balloons filled with an appropriate radionuclide soln. such as of 188Re, attached to catheter are being studied. 166Ho has comparable radionuclidic properties to that of 188Re, can be more easily produced and hence is an attractive alternative to 188Re. Ethylene dicysteine complex of 166Ho was prepd. and its pharmacol. behavior studied. Optimum conditions for the prepn. of complex with respect to the reaction time, ligand concn., pH of the reaction mixt. as well as reaction temp. were standardized. The stability of the labeled complex at room temp. as well as at 4.degree.C was detd. Biodistribution pattern of the injected complex in Wistar rats was estd. at 10 min, 30 min and 3 h post injection. This study indicated that >90% of the injected 166Ho-EC complex was excreted in urine within 3 h post injection, with insignificant retention in any major **organ**. These studies reveal that 166Ho-EC could be a viable substitute for 188Re compds. in radioactive liq.-filled balloon IVRT.

IT **14344-48-0DP**, L,L-Ethylene dicysteine, 166Ho-labeled
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(prepn. and biodistribution of 166Ho-labeled ethylene dicysteine)

RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)

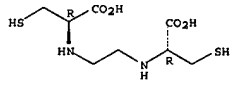
L5 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:244144 CAPLUS
DOCUMENT NUMBER: 135:253846
TITLE: In vivo and in vitro measurement of apoptosis in breast cancer cells using 99mTc-EC-annexin V
AUTHOR(S): Yang, David J.; Azhdarinia, Ali; Wu, Peng; Yu, Dong-Fang; Tansey, Wayne; Kalimi, Saady Kohanim; Kim, E. Edmund; Podoloff, Donald A.
CORPORATE SOURCE: Department of Nuclear Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Cancer Biotherapy & Radiopharmaceuticals (2001), 16(1), 73-83
CODEN: CBRAFJ; ISSN: 1084-9785
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to develop an imaging technique to measure and monitor **tumor** cells undergoing programmed death caused by radiation and chemotherapy using 99mTc-EC-annexin V. Annexin V has been used to measure programmed cell death both in vitro and in vivo. Assessment of apoptosis would be useful to evaluate the efficacy and mechanisms of therapy and disease progression or regression. Ethylenedicysteine (EC) was conjugated to annexin V using sulfo-N-hydroxysuccinimide and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide-HCl as coupling agents. The yield of EC-annexin V was 100%. In vitro cellular uptake, pre- and post-radiation (10-30 Gy) and paclitaxel treatment, was quantified using 99mTc-EC-annexin V. Tissue distribution and planar imaging of 99mTc-EC-annexin V were detd. in breast **tumor**-bearing rats at 0.5, 2, and 4 h. To demonstrate in vivo cell apoptosis that occurred during chemotherapy, a group of rats was treated with paclitaxel and planar imaging studies were conducted at 0.5-4 h. Computer outlined region of interest (ROI) was used to quantify **tumor** uptake on day 3 and day 5 post-treatment. In vitro cellular uptake showed that there was significantly increased uptake of 99mTc-EC-annexin V after irradn. (10-30 Gy) and paclitaxel treatment. In vivo biodistribution of 99mTc-EC-annexin in breast **tumor**-bearing rats showed increased **tumor**-to-blood, **tumor**-to-lung and **tumor**-to-muscle count d. ratios as a function of time. Conversely, **tumor**-to-blood count d. ratios showed a time-dependent decrease with 99mTc-EC in the same time period. Planar images confirmed that the **tumors** could be visualized clearly with 99mTc-EC-annexin. There was a significant difference of ROI ratios between pre- and post-paclitaxel treatment groups at 2 and 4 h post injection. The results indicate that apoptosis can be quantified using 99mTc-EC-annexin and that it is feasible to use 99mTc-EC-annexin to image **tumor** apoptosis.

IT **14344-48-0DP**, LLEthylenedicysteine, 99Tc-labeled annexin V conjugate
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(99mTc-EC-annexin V measurement of apoptosis in breast cancer)

L5 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

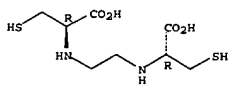
L5 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:868003 CAPLUS
DOCUMENT NUMBER: 135:42804
TITLE: 188Re-ethylene dicysteine: a novel agent for possible use in endovascular radiation therapy
AUTHOR(S): Das, T.; Banerjee, S.; Samuel, G.; Sarma, H. D.; Ramamoorthy, N.; Pillai, M. R. A.
CORPORATE SOURCE: Radiopharmaceuticals Division, Bhabha Atomic Research Centre, Mumbai, 400 085, India
SOURCE: Nuclear Medicine Communications (2000), 21(10), 939-945
CODEN: NMCODC; ISSN: 0143-3636
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several agents, such as 188ReO4-, 188Re-MAG3 and 188Re-DTPA are currently under investigation as radiation sources in liq.-filled balloons for prevention of restenosis following coronary angioplasty. Bearing in mind the risk factor assocd. with leakage of radioactivity in the event of balloon rupture, the criteria sought in selecting suitable agents for endovascular radiation therapy (EVRT) are rapid clearance and low dose to vital **organs**. Since 99Tcm labeled ethylene dicysteine (EC) is a well established agent for renal tubular function imaging, the use of 186Re-ethylene dicysteine as a potential agent for prevention of restenosis after angioplasty has been evaluated previously. Therefore, it was of interest to evaluate the applicability of the more potential isotope of rhenium, 188Re, a high energy .beta.-emitter (E.beta.max = 2.12 MeV) with a suitable T1/2 = 16.9 h, obtainable carrier-free from the 188W-188Re generator, as an attractive and alternative radionuclide for labeling with L,L-EC. In this paper, the prepn. and pharmacol. behavior of the 188Re complex of ethylene dicysteine are reported. The complex can be prepd. in high yields (99.5%) under optimized conditions of pH 2-3, at a ligand concn. of 15 mM, 50 .mu.g (0.18 mM) carrier rhenium and using 2 mg.cntdot.mL-1 stannous chloride. On storage at 4.degree.C, the RC purity was more than 97% after 48 h when prepd. under optimum conditions. Biodistribution studies in Wistar rats showed the desired characteristics of fast blood clearance and low retention of activity in the vital **organs** (<2% in intestine, <1% in stomach, <0.5% in liver) with a high renal excretion (90.65 .+-. 0.6%) at 3 h post-injection. These results confirm the advantages of using the 188Re-EC complex compared with perrhenate and other rhenium radiopharmaceuticals currently being used in balloons for EVRT.

IT **14344-48-0DP**, L,L-Ethylenedicysteine, rhenium-188 complex
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(188Re-ethylene dicysteine: use in endovascular radiotherapy)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)



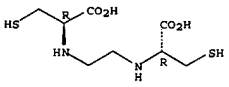
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 15 USPATFULL
ACCESSION NUMBER: 1999:146773 USPATFULL
TITLE: Metal chelates as pharmaceutical imaging agents, processes of making such and uses thereof
INVENTOR(S): Marzilli, Luigi G., Atlanta, GA, United States
Lipowska, Malgorzata, Decatur, GA, United States
Hansen, Lory, Atlanta, GA, United States
Taylor, Jr., Andrew, Atlanta, GA, United States
PATENT ASSIGNEE(S): Emory University, Atlanta, GA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5986074		19991116
APPLICATION INFO.:	US 1997-993219		19971218 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-643413, filed on 6 May 1996, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Gonzalez, Porfirio Nazario
LEGAL REPRESENTATIVE: Greenlee, Winner and Sullivan, P.C.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1,9,12
NUMBER OF DRAWINGS: 14 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 1504
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel metal chelates, exemplified as technetium-99m or rhenium chelates, and to the process of preparing such
metal chelates from corresponding liganda. These ligands and their corresponding metal chelates are synthesized to have a cysteinylethylene
(EC) structure, a monothiourea (MTU) structure, or a dithiourea (DTU) structure. The present invention further relates to a pharmaceutical composition comprising a metal chelate, for example, a .sup.99m Tc-chelate, to the use of the composition for renal imaging and examination of renal function, and to a kit for preparing such a composition prior to use.
IT **14344-48-0**, L,L-Ethylenedicysteine
(reactant for prepn. of 99mTc chelate as potential pharmaceutical imaging agent)
RN 14344-48-0 USPATFULL
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

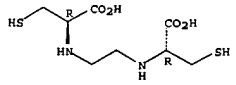
Absolute stereochemistry.



L5 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:328157 CAPLUS
DOCUMENT NUMBER: 131:127222
TITLE: Noninvasive assessment of **tumor hypoxia** with 99mTc labeled metronidazole
AUTHOR(S): Yang, David J.; Ilgan, Seyfettin; Higuchi, Tetsuya; Zareneyrizi, Fereshteh; Oh, Chang-Sok; Liu, Chun-Wei; Kim, E. Edmund; Podoloff, Donald A.
CORPORATE SOURCE: Department of Nuclear Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Pharmaceutical Research (1999), 16(5), 743-750
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The assessment of **tumor hypoxia** by imaging modality prior to radiation therapy would provide a rational means of selecting patients for treatment with radiosensitizers or bioreductive drugs. This study aimed to develop a 99mTc-labeled metronidazole (MN) using ethylenedicysteine (EC) as a chelator and evaluate its potential use to image **tumor hypoxia**. EC was conjugated to amino analog of MN using sulfo-N-hydroxysuccinimide and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide-HCl as coupling agents, the yield was 55%. Tissue distribution of 99mTc-EC-MN was detd. in breast **tumor** -bearing rats at 0.5, 2, and 4 h. Planar imaging and whole-body autoradiograms were performed. The data was compared to that using 99mTc-EC (control), [18P]fluoromisonidazole (FMISO) and [131I] iodomisonidazole (IMISO). In vivo biodistribution of 99mTc-EC-MN in breast **tumor**-bearing rats showed increased **tumor** -to-blood and **tumor**-to-muscle ratios as a function of time. Conversely, **tumor**-to-blood values showed time-dependent decrease with 99mTc-EC in the same time period. Planar images and autoradiograms confirmed that the **tumors** could be visualized clearly with 99mTc-EC-MN from 0.5 to 4 h. There was no significant difference of **tumor**-to-blood count ratios between 99mTc-EC-MN and [131I]IMISO at 2 and 4 h postinjection. From 0.5 to 4 h, both 99mTc-EC-MN and [131I]IMISO have higher **tumor**-to-muscle ratios compared to [18]FMISO. It is feasible to use 99mTc-EC-MN to image **tumor hypoxia**.
IT **14344-48-0**, L,L-Ethylenedicysteine
RL: RCT (Reactant); RACT (Reactant or reagent)
(noninvasive assessment of **tumor hypoxia** with 99mTc-labeled metronidazole)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

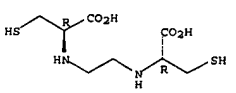
Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS

L5 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:631503 CAPLUS
DOCUMENT NUMBER: 131:348583
TITLE: Synthesis of [99mTc]ethylenedicysteine-colchicine for evaluation of antiangiogenic effect
AUTHOR(S): Zareneyrizi, Fereshteh; Yang, David J.; Oh, Chang-Sok;
Ilgan, Seyfettin; Yu, Dong-Fang; Tansey, Wayne; Liu, Chun-Wei; Kim, E. Edmund; Podoloff, Donald A.
CORPORATE SOURCE: Divisions of Diagnostic Imaging, University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Anti-Cancer Drugs (1999), 10(7), 685-692
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Angiogenesis is in part responsible for **tumor** growth and the development of metastasis. Radiolabeled angiogenesis inhibitors would be useful to assess **tumor** microvasculature d. Colchicine (COL), a potent antiangiogenic agent, is known to inhibit microtubule polymn. and cell arrest at metaphase. This study aimed to develop 99mTc-labeled COL (EC-COL) using ethylenedicysteine (EC) as a chelator to assess **tumor** microvascular d. EC was conjugated to trimethylcolchicinic acid using N-hydroxysuccinimide and 1-ethyl-3-dimethylaminopropyl carbodiimide as coupling agents with a yield of 50-60%. In vivo stability
was analyzed in rabbit serum at 0.5-4 h. Tissue distribution and planar imaging studies of [99mTc]EC-COL were evaluated in breast **tumor** -bearing rats at 0.5, 2 and 4 h. The data was compared to that using [99mTc]EC (control). The radiochem. yield of [99mTc]EC-COL was greater than 95%. [99mTc]EC-COL was stable in rabbit serum. In vivo biodistribution of [99mTc]EC-COL in breast **tumor**-bearing rats showed increased **tumor**-to-blood (0.52 .+-. 0.12 to 0.72 .+-. 0.07) and **tumor**-to-muscle (3.47 .+-. 0.40 to 7.97 .+-. 0.93) ratios as a function of time. Conversely, **tumor**-to-blood values showed a time-dependent decrease with [99mTc]EC over the same time period.
Planar images confirmed that the **tumors** could be visualized clearly with [99mTc]EC-COL from 0.5 to 4 h. [99mTc]EC-COL may be useful to assess antiangiogenic and therapeutic effects during chemotherapy.
IT **14344-48-0P**, L,L-Ethylenedicysteine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of [99mTc]ethylenedicysteine-colchicine for imaging **tumor** microvascular d. and assessing antiangiogenic effect)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



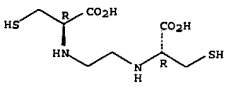
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)

L5 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:512218 CAPLUS
DOCUMENT NUMBER: 131:286782
TITLE: Synthesis and evaluation of .beta.-homocysteine derivatives of 99mTc-L,L-EC and 99mTc-L,L-ECD
AUTHOR(S): Mang'era, K. O.; Verbruggen, A.
CORPORATE SOURCE: Laboratory of Radiopharmaceutical Chemistry, K.U. Leuven, Louvain, B-3000, Belg.
SOURCE: J. Labelled Compd. Radiopharm. (1999), 42(7), 683-699
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bis-amine bis-thiol tetra-ligands such as ethylene dicysteine (EC) and its di-Et ester (ECD) bind 99mTc efficiently at room temp. and neutral to alk. pH to form stable complexes. The use of bis-amine bis-thiol ligands as bifunctional chelating agents (BCAs) for labeling of bioactive compds. (**peptides**, diphosphonates, etc.) looks promising. To study the effect of extending the carboxylic side-group in 99mTc-L,L-EC and 99mTc-L,L-ECD, the authors have synthesized ethylene bis-L-.beta.-homocysteine (L,L-EhC) and its di-Et ester deriv. L,L-EhCD, incorporating a methylene group between each of the carboxyl groups and the N2S2 tetra-ligand core. The more distant carboxyl groups could offer reduced steric hindrance in the use of L,L-EhC and L,L-EhCD as BCAs. As for 99mTc-L,L-ECD, 99mTc-L,L-EhCD is neutral on electrophoresis at pH 6.0. In mice, brain uptake of 99mTc-L,L-EhCD is lower the 99mTc-L,L-ECD. Blood clearance of the two complexes is similar. The diacid 99mTc-L,L-EhC migrates to the same extent as the corresponding 99mTc-L,L-EC on electrophoresis at pH 3.2, 9.0 and 12, but it migrates 25% further at pH 6. Urine levels for 99mTc-L,L-EhC in mice are lower than those for 99mTc-L,L-EC (65% vs. 74% of I.D. at 10 min p.i. and 85% vs. 95% at 30 min p.i., resp.). The results show that the .beta.-homocysteine derivs. retain the key characteristics of 99mTc-L,L-EC and 99mTc-L,L-ECD, i.e. easy formation of stable complexes with 99mTc, a high urinary excretion for 99mTc-L,L-EhC, and in the case of 99mTc-L,L-EhCD a neutral compd. with appreciable brain uptake. These properties indicate that L,L-EhC and L,L-EhCD merit further evaluation as BCAs with attractive conjugation properties.
IT **14344-48-0DP**, 99mTc-complex
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and evaluation of as radiopharmaceuticals)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

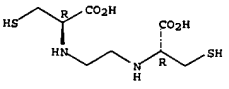
Absolute stereochemistry.

L5 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT **14344-48-0**
RL: RCT (Reactant)
(reaction of in the synthesis and evaluation of .beta.-homocysteine derivs. of 99mTc-L,L-EC and 99mTc-L,L-ECD)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
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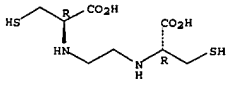
L5 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:159902 CAPLUS
DOCUMENT NUMBER: 132:302450
TITLE: Ethylene dicysteine (EC) and ethyl cysteinate dimer (ECD) complexes of Ga(III) and In(III)
AUTHOR(S): Chattopadhyay, Sankha; Das, M. K.; Sarkar, B. R.; Ramamoorthy, N.
CORPORATE SOURCE: Radiopharmaceuticals Laboratory of BRIT, Variable Energy Cyclotron Centre, Calcutta, 700 064, India
SOURCE: Journal of Radioanalytical and Nuclear Chemistry (1999), 242(1), 29-32
CODEN: JRNCDM; ISSN: 0236-5731
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ethylene dicysteine (EC) and Et cysteinate dimer (ECD) complexes of 67Ga and 111In were prepd. and the complexation yield and radiochem. purity estd. by paper chromatog., paper electrophoresis and solvent extn. into CHCl3. 111In-EC is anionic, whereas 111In-ECD was neutral, EC complexes of 67Ga and 111In were stable up to 6 h and expectedly less lipophilic than ECD complexes. ECD complexes of 67Ga and 111In were unstable in aq. medium, but highly stable in CHCl3. The utility of the work for stabilization of products as **org.** ext. and the possible role and limitation for the development of new 68Ga radiopharmaceuticals and of bifunctional chelating agent (BCA) for 111In are discussed.
IT **14344-48-0DP**, L,L-Ethylenedicysteine, gallium-67 and indium-111 complexes
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn., radiochem. purity and chem. stability in **org.** medium)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:125562 CAPLUS
DOCUMENT NUMBER: 130:334722
TITLE: 99mTc-ethylenedicysteine-**folate**: A new **tumor** imaging agent. Synthesis, labeling and evaluation in animals
AUTHOR(S): Ilgan, Seyfettin; Yang, David J.; Higuchi, Tetsuya; Zareneyrizi, Fereshteh; Bayhan, Hikmet; Yu, Dongfang; Kim, E. Edmund; Podoloff, Donald A.
CORPORATE SOURCE: Department of Nuclear Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Cancer Biother. Radiopharm. (1998), 13(6), 427-435
CODEN: CBRAFJ; ISSN: 1084-9785
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

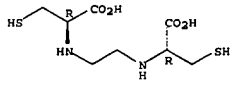
AB It is known that membrane folic acid receptors are responsible for cellular accumulation of **folate** and **folate** analogs such as methotrexate and overexpressed on various **tumor** cells. However, these receptors are highly restricted in normal differentiated tissues. Results of limited in vitro and in vivo animal studies suggest that **folate** receptors could be a potential target for **tumor** imaging. This study aimed to develop a 99mTc-labeled folic acid using ethylenedicysteine (EC) as a chelator and evaluate its labeling efficiency and potential use as a **tumor** seeking agent. Tissue distribution of 99mTc-EC-**folate** was detd. in breast **tumor**-bearing rats at 20 min, 1, 2, and 4 h (n=3/time interval, 370 KBq/rat, i.v.). Blocking study was employed to det. receptor-mediated process; 99mTc-EC-**folate** was co-administrated with 50 and 150 .mu.mol/kg of cold folic acid to **tumor**-bearing rats. Planar imaging and whole-body autoradiograms were performed. The data was compared to that using 99mTc-EC (control). In animal studies, **tumor**/blood count d. ratios at 20 min-4 h increased from 0.81.+-.0.09 to 1.23.+-.0.13 with 99mTc-EC-**folate**. Conversely, these values showed time-dependent decrease from 0.77.+-.0.32 to 0.65.+-.0.01 with 99mTc-EC in the same time period. **Tumor** /muscle and **tumor**/blood count d. ratios significantly decreased with folic acid co-administrations. Planar images and autoradiograms confirmed that the **tumors** could be visualized clearly with 99mTc-EC-**folate**.

IT **14344-48-0**, L,L-Ethylenedicysteine
RL: RCT (Reactant)
(reactant; synthesis of, biodistribution of and **tumor** imaging with 99mTc-ethylenedicysteine-**folate**)

RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 15 USPATFULL
ACCESSION NUMBER: 95:62456 USPATFULL
TITLE: Ester-substituted diaminedithiols and radiolabeled complexes thereof
INVENTOR(S): Bergstein, Paul L., Norwood, MA, United States
Cheesman, Edward H., Townsend, MA, United States
Watson, Alan D., Andover, MA, United States
PATENT ASSIGNEE(S): The Du Pont Merck Pharmaceutical Company, Wilmington, DE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5431900		19950711
APPLICATION INFO.:	US 1993-139894		19931020 (8)

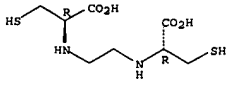
RELATED APPLN. INFO.: Division of Ser. No. US 1988-143561, filed on 26 Jan 1988, now patented, Pat. No. US 5279811 which is a continuation-in-part of Ser. No. US 1987-16982, filed on 18 Feb 1987, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wu, Sean M.
LEGAL REPRESENTATIVE: Boudreaux, Gerald J.
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 833
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Radiopharmaceuticals consisting essentially of a lipophilic, charge neutral radionuclide complex of a diaminedithiol ligand having 1-4 ester groups of the formula --A--COOR where A is a straight or branched chain alkylene of 0-10 carbon atoms and R is an alkyl group of 1-10 carbon atoms are useful in radioimaging brain perfusion in primates. Ester-substituted diaminedithiols in sterile, pharmaceutically acceptable form, and kits of the diaminedithiols and sterile, non-pyrogenic reducing agents for reducing preselected radionuclides are also provided. Technetium-99m is a preferred radionuclide.

IT **14344-48-0P**
(prepn. and reaction of, in prepn. of ester-substituted diaminedithiol for radiopharmaceutical for brain imaging)

RN 14344-48-0 USPATFULL
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



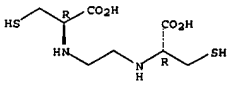
L5 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 1995:485112 CAPLUS
DOCUMENT NUMBER: 123:144521
TITLE: N,N'-Ethylene-di-L-cysteine (EC) complexes of Ga(III) and In(III): molecular modeling, thermodynamic stability, and in vivo studies
AUTHOR(S): Anderson, Carolyn J.; John, Christy S.; Li, Yuejin J.; Hancock, Robert D.; Mccarthy, Timothy J.; Martell, Arthur E.; Welch, Michael J.
CORPORATE SOURCE: School of Medicine, Washington University, St Louis, MO, 63110, USA
SOURCE: Nucl. Med. Biol. (1995), 22(2), 165-73
CODEN: NMBIEO; ISSN: 0883-2897
DOCUMENT TYPE: Journal
LANGUAGE: English

AB L,L-Ethylenedicysteine (EC) is a N2S2 ligand that also contains two carboxylic acid moieties for complexation of Ga(III) and In(III) in a hexacoordinate environment. The stability consts. of Ga- and In-EC have been detd. by potentiometric methods. The stability of In-EC was found to be greater than that of Ga-EC, with stability consts. (log K's) of 33.0 and 31.5, resp. A mol. mechanics evaluation of the Ga- and In-EC complexes support the thermodn. results. 67Ga- and 111In-labeled complexes of EC were prepd. and analyzed by thin layer chromatog. and electrophoresis. Both complexes were evaluated in biodistribution studies in normal Sprague-Dawley rats. 111In-EC cleared rapidly through the hepatobiliary system, whereas 67Ga-EC remained in the liver at 1 h post-injection. Although 67Ga-EC was retained in the liver, suggesting instability of the complex in vivo, 67Ga-EC was stable in rat plasma in vivo at 2 h post-injection. Because of the high thermodn. and in vivo stability of In-EC, derivs. of EC may have applications as bifunctional chelates for 111In-labeled proteins and **peptides**. More lipophilic analogs of 68Ga-EC may also have potential as myocardial PET imaging agents.

IT **14344-48-0**, N,N'-Ethylenedi-L-cysteine
RL: PRP (Properties)
(MO, thermodn. stability, and in vivo studies of ethylenedicysteine complexes of gallium and indium)

RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

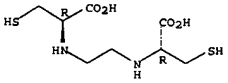


L5 ANSWER 13 OF 15 USPATFULL
ACCESSION NUMBER: 94:5666 USPATFULL
TITLE: Ester-substituted diaminedithiols and radiolabeled complexes thereof
INVENTOR(S): Bergstein, Paul L., Norwood, MA, United States
Cheesman, Edward H., Townsend, MA, United States
Watson, Alan D., Andover, MA, United States
PATENT ASSIGNEE(S): The Du Pont Merck Pharmaceutical Company, Wilmington, DE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5279811		19940118
APPLICATION INFO.:	US 1988-143561		19880126 (7)

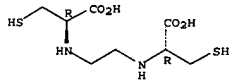
DISCLAIMER DATE: 20080318
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1987-16982, filed on 18 Feb 1987, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Stoll, Robert L.
ASSISTANT EXAMINER: Covert, John M.
LEGAL REPRESENTATIVE: Boudreaux, Gerald J.
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
LINE COUNT: 884
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Radiopharmaceuticals consisting essentially of a lipophilic, charge neutral radionuclide complex of a diaminedithiol ligand having 1-4 ester
groups of the formula --A--COOR where A is a straight or branched chain alkylene of 0-10 carbon atoms and R is an alkyl group of 1-10 carbon atoms are useful in radioimaging brain perfusion in primates. Ester-substituted diaminedithiols in sterile, pharmaceutically acceptable form, and kits of the diaminedithiols and sterile, non-pyrogenic reducing agents for reducing preselected radionuclides are
also provided. Technetium-99m is a preferred radionuclide.
IT **14344-48-0P**
(prepn. and esterification of)
RN 14344-48-0 USPATFULL
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:239232 CAPLUS
DOCUMENT NUMBER: 120:239232
TITLE: Technetium-99m labeling on monoclonal **antibodies** via N,N'-ethylene-bis-L-cysteine
AUTHOR(S): Qu, Tong; Wu, Yonghui; Wang, Xiangyun; Liu, Yuanfang; Ye, Yunhua; Wu, Chuanchu
CORPORATE SOURCE: Dep. Tech. Phys., Peking Univ., Beijing, Peop. Rep. China
SOURCE: Radiochim. Acta (1993), 63, 209-12
CODEN: RAACAP; ISSN: 0033-8230
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new developed excellent kidney imaging agent, N,N'-ethylene-bis-L-cysteine (EC) has been used as a bifunctional chelating agent (BFCA) for Tc-99m labeling of monoclonal **antibodies** (MoAb). A new conjugation agent N-hydroxyl-1,4-epoxylcyclohex-5-ene-2,3-di-carboxyl-imide (HONCE) and a water-sol. dehydrating agent 1-ethyl-3-(3-dimethylaminopropyl)carbo-diimide (EDC) were used to accomplish the conjugation of EC with **antibodies**. A conjugation yield of 30-40% was obtained. The exptl. conditions were optimized for the best conjugation performance. Tc-99m labeling was then completed after conjugation. More than 80% of the immunoreactivity was retained by monoclonal **antibodies** conjugated with EC. More than 70% of the radioactivity was retained in the labeled complex Tc-99m-EC-Ab after incubation in fresh EC and cysteine solns. for 16-20 h. The biodistributions of labeled **antibody** in mice were also detd.
IT **14344-48-0DP**, technetium-99-monoclonal **antibody** complexes
RL: BOC (Biological occurrence); SPN (Synthetic preparation); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(prepn. and biodistribution of, imaging in relation to)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 15 OF 15 USPATFULL
ACCESSION NUMBER: 90:38223 USPATFULL
TITLE: Technetium -99m complex for examining the renal function
INVENTOR(S): Nosco, Dennis L., Florissant, MO, United States
Verbruggen, Alfons M., Leuven, Belgium
PATENT ASSIGNEE(S): Mallinckrodt, Inc., St. Louis County, MO, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4925650		19900515
APPLICATION INFO.:	US 1988-272177		19881116 (7)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Maples, John S.
LEGAL REPRESENTATIVE: Hay, David A., Klostermann, Roy J.
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 575
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a technetium-99m complex of the general formula
##STR1## wherein Z is a sulphur atom or an amino group of the general formula R.sub.17 --N--(R.sub.18).sub.k, in which k is 0 or 1 and R.sub.17 and R.sub.18 have the same meanings as the symbols R.sub.1 -R.sub.16 ;

each of the symbols R.sub.1 -R.sub.16 is individually selected from the group consisting of hydrogen, straight or branched, unsubstituted or substituted alkyl having 1-4 carbon atoms, and ACOOH, wherein A is a straight or branched, unsubstituted or substituted alkly group having 0-4 carbon atoms;

and R.sub.5 together with R.sub.6 or R.sub.9 together with R.sub.10 additionally may form an oxygen atom;

Tc represents technetium-99m;

t is 0 or 1; and

n is 0 or 1;

with the provisos that

(a) if R.sub.15, R.sub.16, R.sub.17 and/or R.sub.18 are/is ACOOH, A is a
straight or branched, unsubstituted or substituted alkyl group having 1-4 carbon atoms;

(b) at least one of the symbols R.sub.1 -R.sub.18 is ACOOH; and

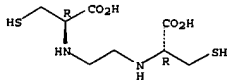
(c) if t is 1, at least two of the symbols R.sub.1 -R.sub.18 are ACOOH;

or a pharmaceutically acceptable salt of this compound.

The invention further relates to a radiopharmaceutical composition comprising said complex, to the use of this composition for examining the renal function, and to a kit for preparing such a composition.
IT **14344-48-0DP**, technetium-99 complexes

L5 ANSWER 15 OF 15 USPATFULL (Continued)
(prepn. and biodistribution of)
RN 14344-48-0 USPATFULL
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L1             1 S E3

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     19 APR 2002
L2            49 S L1
L3            45 DUP REM L2 (4 DUPLICATES REMOVED)
L4            16 S L2 AND (ANTI(W)CANCER? OR DNA OR ANTI(W)METABOLIT? OR TUMOR?
L5            15 DUP REM L4 (1 DUPLICATE REMOVED)

=> s l2 and (imag?)
L6            28 L2 AND (IMAG?)

=> s l6 not l4
L7            15 L6 NOT L4

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8            15 DUP REM L7 (0 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):y
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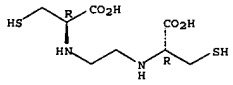
L8 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:931407 CAPLUS
DOCUMENT NUMBER: 136:196262
TITLE: Development of a Conjugate of 99mTc-EC with Aminomethylenediphosphonate in the Search for a Bone Tracer with Fast Clearance from Soft Tissue
AUTHOR(S): Verbeke, Kristin; Rozenski, Jef; Cleynhens, Bernard; Vanbilloen, Hubert; de Groot, Tjibbe; Weyns, Nancy; Bormans, Guy; Verbruggen, Alfons
CORPORATE SOURCE: Laboratory of Radiopharmaceutical Chemistry, University Hospital Gasthuisberg, Louvain, B-3000, Belg.
SOURCE: Bioconjugate Chemistry (2002), 13(1), 16-22
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB For the currently used 99mTc-labeled diphosphonates such as 99mTc-MDP and 99mTc-HDP, the required interval of 2.5 to 3 h between injection and the scintigraphic bone **imaging** is an inconvenience. The present study was set up in an attempt to develop a technetium-99m-labeled diphosphonate with efficient bone uptake and more rapid clearance from blood and soft tissue by renal extn. and excretion so that it would be possible to start **imaging** as early as 1 h after injection. A conjugate of the new renal tracer agent 99mTc-ethylene dicysteine (99mTc-L,L-EC), covalently bound via one of its carboxylates with aminomethylenediphosphonic acid (AMDP), was synthesized in seven steps. EC-AMDP could be labeled easily and efficiently with 99mTc at pH .gtoreq.12 and room temp. Anal. using ion pair reversed phase high performance liq. chromatog. showed the formation of a mixt. of two main compds. with reproducible relative ratios, which were stable as a function of time. In a baboon, the scintigraphic **images** obtained with the new agent showed good quality bone scans, with clear visualization of the skeleton and low soft tissue activity at resp. 1 and 2 h after injection.
IT **14344-48-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of ethylene dicysteine diphosphonate complex of 99mTc for bone scintigraphy)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

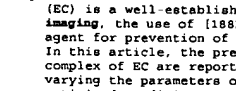


REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)

L8 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:255982 CAPLUS
DOCUMENT NUMBER: 133:219567
TITLE: [186/188Re] rhenium-ethylene dicysteine (Re-Ec): preparation and evaluation for possible use in endovascular brachytherapy
AUTHOR(S): Das, T.; Banerjee, S.; Samuel, G.; Kothari, K.; Unni, P. R.; Sarma, H. D.; Ramamoorthy, N.; Pillai, M. R. A.
CORPORATE SOURCE: Radiopharmaceuticals Division Bhabha Atomic Research Centre, Mumbai, India
SOURCE: Nuclear Medicine and Biology (2000), 27(2), 189-197
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 188ReO4-, 188Re-MAG3, and 188Re-DTPA are currently under investigation as radiation sources in liq.-filled balloons for prevention of restenosis following coronary angioplasty. Because 99mTc-labeled ethylene dicysteine (EC) is a well-established agent for renal tubular function **imaging**, the use of [188Re] rhenium-labeled EC as a potential agent for prevention of restenosis after angioplasty is worth evaluation. In this article, the prepn. and pharmacol. behavior of [188/186Re]Re complex of EC are reported. The yield of the Re complex was optimized by varying the parameters of complexation. The complex prepd. under the optimized conditions was found to be stable over a period of 7 days when stored at pH 2 and at 4.degree.C. The pharmacol. behavior of [188/186Re]Re-EC confirms its similarity to 188Re-MAG3 and its superiority over 188ReO4- for use in endovascular brachytherapy.
IT **14344-48-0P**, L,L-Ethylene dicysteine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
([186/188Re] rhenium-ethylene dicysteine: prepn. and evaluation for possible use in endovascular brachytherapy)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

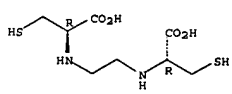
Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:770468 CAPLUS
DOCUMENT NUMBER: 134:322832
TITLE: Study of various esters of ethyl cysteine acid dimer as brain perfusion **imaging** agents and formulation into single vial kit for labeling with 99mTc
AUTHOR(S): Afshan, A.; Jehangir, M.; Amin, W.; Mujahid, A.
CORPORATE SOURCE: RadioIsotope Production Group, Nuclear Chemistry Division, Pakistan Institute of Science and Technology, Nilore, Pak.
SOURCE: Nuclear Science Journal (2000), 37(3), 188-196
CODEN: HTKHAB; ISSN: 0029-5647
PUBLISHER: Nuclear Science Journal
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two analogs of Et cysteinate dimer (ECD) namely Pr cysteinate dimer (PCD) and Bu cysteinate dimer (BCD) have been synthesized and characterized. The optimization of parameters required to produce "single vial kit" of these analogs to obtain the stable complexes by labeling with 99mTc have also been carried out. Different anal. techniques were used for the quality control of 99mTc-PCD and 99mTc-BCD complexes prepd. from the freeze dried PCD and BCD kits resp. The difference in procedures of synthesis, formulation of kits and their quality control were compared with ECD. The KD of ECD and its analogs was also studied. Biodistribution studies in mice, sacrificed 1.0 min after injection showed brain uptake of 99mTc-ECD as 5.0 .+-. 0.5%, 99mTc-PCD as 4.3 .+-. 0.3% and 99mTc-BCD as 1.6 .+-. 0.7%. These complexes were also studied in monkeys prior to clin. evaluations in humans. The pharmacodynamic study of 99mTc-ECD showed that time of max. uptake in the brain was between 30 s. to 1 m. and the retention of activity was maintained for 3 h after injection. 99mTc-PCD showed that the time of its max. uptake in the brain was 2 m and the retention of the activity was maintained even 2.5 h post injection which was sufficient time to perform SPET studies as it showed high brain/blood contrast. On the other hand 99mTc-BCD did not give favorable results of biodistribution as a brain perfusion **imaging** agent in the rhesus monkey.
IT **14344-48-0**, L-Cysteine, N,N'-1,2-ethanediylbis-
RL: RCT (Reactant); RACT (Reactant or reagent)
(cysteinate dimer analogs effects as brain perfusion **imaging** agents and formulation into single vial kit for labeling with 99mTc)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

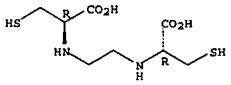
L8 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)

L8 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:733055 CAPLUS
DOCUMENT NUMBER: 131:345771
TITLE: Preparation of metal chelates as pharmaceutical **imaging** agents
INVENTOR(S): Marzilli, Luigi G.; Lipowska, Malgorzata; Hansen, Lory; Taylor, Andrew, Jr.
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: U.S., 32 pp., Cont.-in-part of U.S. Ser. No. 643,413, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5986074	A	19991116	US 1997-993219	19971218
US 5955053	A	19990921	US 1996-643413	19960506

PRIORITY APPLN. INFO.: US 1996-643413 19960506
OTHER SOURCE(S): MARPAT 131:345771
AB The present invention relates to novel metal chelates, exemplified as technetium-99m or rhenium chelates, and to the process of prepg. such metal chelates from corresponding ligands. These ligands and their corresponding metal chelates were synthesized to have a cysteinylethylene (EC) structure, a monothiourea (MTU) structure, or a dithiourea (DTU) structure. Thus, 99mTcO(CEMA) [H3CEMA = HSCH2CH(COOH)NHCH2CH2NHC(O)CH2SCH2Ph], was prepd. and biodistribution studied for four isomeric forms of the complex (syn- and anti-, D and L). The present invention further relates to a pharmaceutical compn. comprising a metal chelate, for example, a 99Tc-chelate, to the use of the compn. for renal **imaging** and examn. of renal function, and to a kit for prepg. such a compn. prior to use.
IT **14344-48-0**, L,L-Ethylenedicysteine
RL: RCT (Reactant)
(reactant for prepn. of 99mTc chelate as potential pharmaceutical **imaging** agent)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

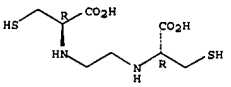


REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)

L8 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:472510 CAPLUS
DOCUMENT NUMBER: 125:136612
TITLE: Indium(III) and gallium(III) complexes of bis(aminoethanethiol) ligands with different denticities: Stabilities, molecular modeling, and in vivo behavior. [Erratum to document cited in CA124:111212]
AUTHOR(S): Sun, Yizhen; Anderson, Carolyn J.; Pajeau, Tammy S.; Reichert, David E.; Hancock, Robert D.; Motekaitis, Ramunas J.; Martell, Arthur E.; Welch, Michael J.
CORPORATE SOURCE: Dep. Chem., Texas A and M Univ., College Station, TX, 77843-3255, USA
SOURCE: J. Med. Chem. (1996), 39(12), 2434
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The errors were not reflected in the abstr. or the index entries.
IT **14344-48-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(indium(III) and gallium(III) complexes of bis(aminoethanethiol) ligands with different denticities: prepn., stabilities, mol. modeling,
and in vivo behavior for diagnostic **imaging** (Erratum))
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

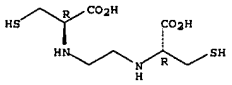
Absolute stereochemistry.



L8 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:6882 CAPLUS
DOCUMENT NUMBER: 124:111212
TITLE: Indium(III) and Gallium(III) Complexes of Bis(aminoethanethiol) Ligands with Different Denticities: Stabilities, Molecular Modeling, and in Vivo Behavior
AUTHOR(S): Sun, Yizhen; Anderson, Carolyn J.; Pajeau, Tammy S.; Reichert, David E.; Hancock, Robert D.; Motekaitis, Ramunas J.; Martell, Arthur E.; Welch, Michael J.
CORPORATE SOURCE: Department of Chemistry, Texas A and M University, College Station, TX, 77843-3255, USA
SOURCE: J. Med. Chem. (1996), 39(2), 458-70
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Complexes of Ga(III) and In(III) radionuclides are widely used in diagnostic **imaging**. In this study, the following ligands of denticities 4, 5, and 6, resp., were prepd.: N,N'-bis(2,2-dimethyl-2-mercaptoethyl)ethylenediamine (4SS), 1-carboxy-N,N'-bis(2,2-dimethyl-2-mercaptoethyl)ethylenediamine (5SS), and N,N'-bis(2,2-dimethyl-2-mercaptoethyl)ethylenediamine-N,N'-diacetic acid (6SS). Syntheses of the two new ligands, 5SS and 6SS, are described. Equil. consts. for their In(III) and Ga(III) complexes were detd. by both direct and ligand-competitive potentiometric methods. The formation const. (KML = {ML}/{M}{L}) of In(III)-6SS in 0.100 M KNO3 at 25.0.degree.C is 1039.8, and its pM at physiol. pH (7.4 with 100% excess of the ligand) is 30.9. These values are higher than those of any other previous reported ligand for In(III). The stability consts. of the complexes of 4SS, 5SS, 6SS, and the analogous ligand EDDASS, N,N'-bis(2-mercaptoethyl)ethylenediamine-N,N'-diacetic acid, which does not contain gem-di-Me groups, are compared. The thermodn. stabilities of the In(III) complexes of all ligands except 6SS are greater than those of the corresponding Ga(III) complexes. The presence of the geminol di-Me groups in 6SS increased the stability of the Ga(III) and In(III) complexes over those of EDDASS. The effects of the gem-di-Me groups on complex stabilities are explained by mol. modeling. The serum stabilities and biodistributions out to 1 h postinjection of 67/68Ga and 111In chelates of 4SS, 5SS, and 6SS were measured and compared with those of EDDASS. The 67/68Ga- and 111In-ligand complexes with more donor atoms showed were more stable in serum, both in vitro and in vivo. The biodistributions of the 67/68Ga- and 111In-ligand complexes exhibited distinct trends. None of the 67/68Ga- and 111In-chelates demonstrated significant heart or brain uptake. The majority of uptake for all compds. was in the liver and kidney. The degree of clearance through the liver corresponded to the thermodn. stability of the complex. Correlations between in vivo behavior, mol. modeling data, and thermodn. stability of the complexes are discussed.
IT **14344-48-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(indium(III) and gallium(III) complexes of bis(aminoethanethiol) ligands with different denticities: prepn., stabilities, mol. modeling,

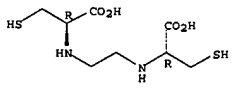
L8 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)
and in vivo behavior for diagnostic **imaging**)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



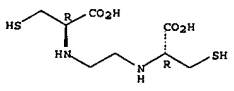
L8 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:860007 CAPLUS
DOCUMENT NUMBER: 124:4094
TITLE: Kinetic study on ligand exchange reaction between EC and 99mTc-GH
AUTHOR(S): Wu, Chunying; Luo, Shineng; Fang, Ping; Huang, Heyun; Xie, Minhao; Meng, Hong
CORPORATE SOURCE: State Key Laboratory Nuclear Medicine, Jiangsu Institute Nuclear Medicine, Wuxi, 214063, Peop. Rep. China
SOURCE: Hejishu (1995), 18(5), 293-6
CODEN: NUTEDL; ISSN: 0253-3219
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The ligand exchange reaction between EC (N,N'-ethylene-di(L-cysteine)) and 99mTc-GH and its influence factors such as concns. of EC and pH were described in this paper. The concn. of EC has no influence on the exchange reaction rate const., while pH is the most important influence factor. The rate consts. of ligand exchange reaction at different pH values were detd. The results showed that to make the labeling yield of the kidney contrast agent 99mTc-EC higher than 90%, pH of the reaction must be higher than 8.
IT **14344-48-0**, N,N'-Ethylene-di(L-cysteine)
RL: RCT (Reactant)
(kinetic study on ligand exchange reaction between EC and 99mTc-GH)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **14344-48-0DP**, N,N'-Ethylene-di(L-cysteine), technetium complex
RL: SPN (Synthetic preparation); PREP (Preparation)
(kinetic study on ligand exchange reaction between EC and 99mTc-GH)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:765168 CAPLUS
DOCUMENT NUMBER: 123:221923
TITLE: Tetrahydroaminoacridine modulates technetium-99m labeled ethylene dicysteinate retention in Alzheimer's disease measured with single photon emission computed tomography **imaging**
AUTHOR(S): Riekkinen, Paavo Jr.; Kuikka, J.; Soininen, H.; Helkala, E-L.; Hallikainen, M.; Riekkinen, Paavo
CORPORATE SOURCE: Department of Neurology, University and University Hospital of Kuopio, CANTHIA, POB 1627, Kuopio, 70211, Finland
SOURCE: Neurosci. Lett. (1995), 195(1), 53-6
CODEN: NELED5; ISSN: 0304-3940
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigated if acute treatment with tetrahydroaminoacridine (THA) (25 or 75 mg, p.o.) affects technetium-99m labeled ethylene dicysteinate (ECD) retention abnormalities in patients with mild to moderate Alzheimer's disease (AD; mean age 69 yr). THA (75 mg) increased temporal, prefrontal and occipital ECD retention (normalized to cerebellum) in mildly demented AD patients, but 25 mg of THA had no effect on ECD retention. After 75 mg THA, prefrontal and temporal ECD retention correlated with improved executive and memory functioning, resp. THA (25 or 75 mg) had no measurable effect on ECD retention of moderately demented patients.
IT **14344-48-0D**, labeled with technetium-99m
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(tetrahydroaminoacridine modulates technetium-99m labeled ethylene dicysteinate retention in Alzheimer's disease measured with SPECT)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:264828 CAPLUS
DOCUMENT NUMBER: 120:264828
TITLE: Ester-substituted diaminedithiols and radiolabeled complexes thereof for radio-**imaging** brain
INVENTOR(S): Bergstein, Paul L.; Cheesman, Edward H.; Watson, Alan D.
PATENT ASSIGNEE(S): Du Pont Merck Pharm. Co., USA
SOURCE: U.S., 13 pp. Cont.-in-part of U.S. Ser. No. 16,982, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5279811	A	19940118	US 1988-143561	19880126
AU 8811748	A1	19880901	AU 1988-11748	19880216
AU 614276	B2	19910829		
DK 8800816	A	19880819	DK 1988-816	19880217
EP 279417	A2	19880824	EP 1988-102252	19880217
EP 279417	A3	19890726		
EP 279417	B1	19920520		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 76401	E	19920615	AT 1988-102252	19880217
ES 2042609	T3	19931216	ES 1988-102252	19880217
JP 63295549	A2	19881201	JP 1988-34137	19880218
ZA 8801136	A	19891025	ZA 1988-1136	19880218
CA 1271195	A1	19900703	CA 1988-559230	19880218
US 5431900	A	19950711	US 1993-139894	19931020

PRIORITY APPLN. INFO.: US 1987-16982 19870218
US 1988-143561 19880126
EP 1988-102252 19880217

OTHER SOURCE(S): MARPAT 120:264828

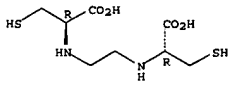
AB Radiopharmaceuticals consisting essentially of a lipophilic, charge neutral radionuclide complex of a diaminedithiol ligand having 1-4 ester groups of the -A-COOR (A = C1-10 alkylene, R = C1-10 alkyl) are prepd. for radioimaging brain perfusion in primates. Technetium-99m is a preferred radionuclide. Thus N,N'-1,2-ethylenediylbis-L-cysteine (I) (prepn. is given) in EtOH was refluxed with HCl gas for 2.5 h, then slurry was cooled, filtered and purified to obtain I.2Et ester 2HCl (II). II and SnCl2 and 99mTcO4 were mixed to obtain 99mTc diaminedithiol complex of the invention. Different 99mTc diaminedithiol complexes were used for evaluation of regional cerebral blood flow by performing brain **imaging** studies in monkeys.

IT **14344-48-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and esterification of)

RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)



L8 ANSWER 10 OF 15 USPATFULL
ACCESSION NUMBER: 93:18562 USPATFULL
TITLE: Silver halide elements with improved speed and low fog
INVENTOR(S): Chan, Dominic M., Wilmington, DE, United States
LeStrange, Raymond J., Hendersonville, NC, United States
PATENT ASSIGNEE(S): E. I. du Pont de Nemours and Company, Wilmington, DE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5192655		19930309
APPLICATION INFO.:	US 1991-726331		19910705 (7)

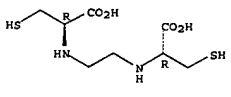
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Bowers, Jr., Charles L.
ASSISTANT EXAMINER: Baxter, Janet C.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 227
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Substituted diaminedithio-containing compounds useful for improving the speed of a silver halide emulsion are described. These compounds can be added in small amounts to the emulsion preferably after the emulsion has been chemically sensitized and just prior to coating. Fog levels are not greatly affected which is surprising since conventional sensitizers generally do increase the fog level.

IT **14344-48-0**
(photog. sensitizer)

RN 14344-48-0 USPATFULL
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



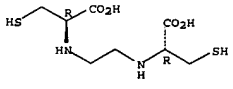
L8 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:403351 CAPLUS
DOCUMENT NUMBER: 117:3351
TITLE: Technetium-99m-L,L-ethylenedicysteine: a renal **imaging** agent. I. Labeling and evaluation in animals
AUTHOR(S): Verbruggen, Alfons M.; Nosco, Dennis L.; Van Nerom, Chris G.; Bormans, Guy M.; Adriaens, Paul J.; De Roo, Michel J.
CORPORATE SOURCE: Lab. Radiopharm. Chem., KU Leuven, Belg.
SOURCE: J. Nucl. Med. (1992), 33(4), 551-7
CODEN: JNMEAQ; ISSN: 0161-5505
DOCUMENT TYPE: Journal
LANGUAGE: English

AB L,L-Ethylenedicysteine (L,L-EC) can be labeled efficiently with 99mTc at pH 12 to obtain a highly pure and very stable tracer agent (99mTc-L,L-EC). The biol. behavior of 99mTc-L,L-EC was studied in mice and a baboon. In mice, 99mTc-L,L-EC demonstrated a more rapid urinary excretion and less retention in the kidneys, the liver, the intestines, and the blood than did 99mTc-MAG3 at 10 and 60 min p.i. Urinary excretion decreased in probenecid pretreated mice, which indicates active tubular transport. In the baboon, the renograms for 99mTc-MAG3 and 99mTc-L,L-EC were comparable. Plasma-protein binding of 99mTc-L,L-EC was lower than that of 99mTc-MAG3 while its distribution vol. and 1-h plasma clearance were clearly higher. The promising results of the animal expts. suggest that 99mTc-L,L-ethylenedicysteine may be a useful alternative to 99mTc-MAG3 for renal function studies in humans.

IT **14344-48-0**
RL: BIOL (Biological study)
(labeling of, with technetium-99m, renal **imaging** in relation to)

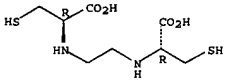
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:55225 CAPLUS
DOCUMENT NUMBER: 118:55225
TITLE: A new renal function **imaging** agent technetium-99m-EC
AUTHOR(S): Zhu, Lin; Chen, Dazhou; Hong, Tao; Zhang, Zheng; Liu, Boli
CORPORATE SOURCE: Natl. Res. Cent., CRM's, Beijing, Peop. Rep. China
SOURCE: Tongweisu (1991), 4(4), 212-16
CODEN: TONGEM; ISSN: 1000-7512
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB EC (N,N'-ethylene-di-L-cysteine, I) was synthesized by a 2-step reaction and labeled with 99mTcO4-. The effects of pH and various quantities of SnCl2 and EC on the labeling yield were studied. The biodistribution in mice was measured.
IT **14344-48-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and technetium-99m labeling of)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:511706 CAPLUS
DOCUMENT NUMBER: 113:111706
TITLE: Technetium-99m complex for examining renal function
INVENTOR(S): Nosco, Dennis L.; Verbruggen, Alfons M.
PATENT ASSIGNEE(S): Mallinckrodt, Inc., USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

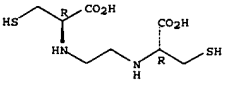
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4925650	A	19900515	US 1988-272177	19881116
IL 92211	A1	19950124	IL 1989-92211	19891103
IL 107560	A1	19961114	IL 1989-107560	19891103
CA 2002850	AA	19900516	CA 1989-2002850	19891114
WO 9005733	A1	19900531	WO 1989-US5132	19891116
W: AU, JP				
RW: AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, SE				
AU 8946489	A1	19900612	AU 1989-46489	19891116
AU 629880	B2	19921015		
EP 444130	A1	19910904	EP 1990-900458	19891116
EP 444130	B1	19980610		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04505152	T2	19920910	JP 1990-500433	19891116
JP 3129431	B2	20010129		
AT 167188	E	19980615	AT 1990-900458	19891116

PRIORITY APPLN. INFO.: US 1988-272177 A 19881116
IL 1989-92211 A3 19891103
WO 1989-US5132 W 19891116

OTHER SOURCE(S): MARPAT 113:111706
AB 99mTc complexes I [Z = S, R17NR18k; R1-18 = H, (un)substituted C1-4 alkyl, ACO2H; A = (un)substituted C0-4 alkyl; R5 and R6 or R9 and R10 = O; Tc = 99mTc; k, t, n = 0, 1; with provisions) or pharmaceutically acceptable salts are used in radiopharmaceutical compds. for examg. renal function. {L,L}-N,N'-Bis(1-carboxy-2-mercaptoethyl)ethylenediamine was reacted with Na [99mTc]-pertechnetate in the presence of SnCl2. The 99mTc diaminodithiol complex was administered i.v. in humans at 0.5 mCi and the radioactivity at the kidneys was recorded by a gamma camera equipped with a high-sensitivity collimator. The max. renal activity was achieved after 2.5 min. After 40 min, 2.9% of the injected dose had accumulated in the liver compared to 4.0% accumulation of 99mTc-mercaptoacetyltriglycine. The renograms of these 2 compds. were approx. identical.
IT **14344-48-0DP**, technetium-99 complexes
RL: BOC (Biological occurrence); SPN (Synthetic preparation); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(prepn. and biodistribution of)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

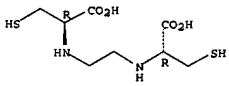
Absolute stereochemistry.

L8 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)



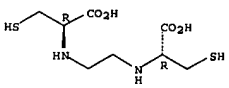
L8 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:499052 CAPLUS
DOCUMENT NUMBER: 115:99052
TITLE: Development of 99mTc-ECD as a new brain **imaging** agent I. Synthesis and labeling
AUTHOR(S): Zhang, Xiaoxiang; Liu, Boli; Jin, Yutai; Kung, Hank F.
CORPORATE SOURCE: Dep. Chem., Beijing Norm. Univ., Beijing, Peop. Rep. China
SOURCE: Tongweisu (1990), 3(2), 73-8
CODEN: TONGEM; ISSN: 1000-7512
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB ECD (Et Cysteinate Dimer) was synthesized by a 2-step reaction. ECD was labeled by the ligand exchange reaction between 99mTc-GH (glucoheptonate) and ECD. The effect of temp., pH value, and various quantities of Ca-GH and SnCl2 on the labeling percentage was studied. The effect of pH value is very important.
IT **14344-48-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and technetium-99m labeling of)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **14344-48-0DP**, technetium-99 complexes
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of metastable, for brain **imaging**)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:435955 CAPLUS
DOCUMENT NUMBER: 111:35955
TITLE: Ester-substituted diaminedithiols and radiolabeled complexes thereof for radioimaging the brain
INVENTOR(S): Bergstein, Paul Louis; Cheesman, Edward Hollister; Watson, Alan David
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 279417	A2	19880824	EP 1988-102252	19880217
EP 279417	A3	19890726		
EP 279417	B1	19920520		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5279811	A	19940118	US 1988-143561	19880126
AT 76401	E	19920615	AT 1988-102252	19880217

PRIORITY APPLN. INFO.: US 1987-16982 19870218
US 1988-143561 19880126
EP 1988-102252 19880217
OTHER SOURCE(S): MARPAT 111:35955

AB Radiopharmaceuticals comprising a lipophilic, charge-neutral radionuclide complex of a diaminedithiol having >1 ester group of ACO2R (A = C0-6 straight or branched alkylene; R = C1-6 alkyl) are prepd. for radioimaging the brain. Ester-substituted diaminedithiols I and II (R1-12 = H, C1-10 alkyl, ACO2R; A = C0-10 straight or branched alkylene; R = C1-10 alkyl, Ph or Bz optionally substituted with .ltoreq.5 ring substituents of C1-4 alkyl, F, etc., or 5-6-membered heterocycle contg. 1-2 heteroatoms of N, O, or S; .gtoreq.1 of R1-12 = ACO2R; n, o, p = 1, 2) in sterile pharmaceutically acceptable form, and kits of the diaminedithiols and sterile, nonpyrogenic reducing agents for reducing preselected radionuclides are also provided. I (R1-2,4-9,11-12 = H; R3,10 = CO2Et) with L, L stereo (II) was added to a mixt. of Na glucoheptonate, SnCl2, and 99mTcO4. The complex was purified by HPLC on a Brownlee RP-8 Spheri 5 column. It had a partition coeff. in octanol/H2O of 44, a rhesus monkey brain extn. % injection dose (detd. by planar **imaging**) of 4.8, brain retention half-life of >1440, and a gray/white matter ratio of 2-3:1. II.2HCl was synthesized from (R)-thiazolidine-4-carboxylic acid in 3 steps.

IT **14344-48-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of ester-substituted diaminedithiol for radiopharmaceutical for brain **imaging**)
RN 14344-48-0 CAPLUS
CN L-Cysteine, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L8 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2002 ACS (Continued)